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(71) Applicants: **CALIPER TECHNOLOGIES CORP.** [US/US]; 605 Fairchild Drive, Mountain View, CA 94043 (US). **AGILENT TECHNOLOGIES INC.** [US/US]; 395 Page Mill Road, Palo Alto, CA 94303 (US).

(72) Inventors: **UNNO, Garrett**; 3460 Rosedale Drive, San Jose, CA 95117 (US). **KENNEDY, Colin, B.**; 413 Ash Street, Mill Valley, CA 94941 (US). **KALTENBACH, Patrick**; Altenbergstrasse 1, D-76476 Bischweier (DE). **BERNDT, Manfred**; Hellenstrasse 55, D-76337 Waldbronn (DE).

(74) Agents: **QUINE, Jonathan, Alan**; The Law Offices of Jonathan Alan Quine, P.O. Box 458, Alameda, CA 94501 et al. (US).

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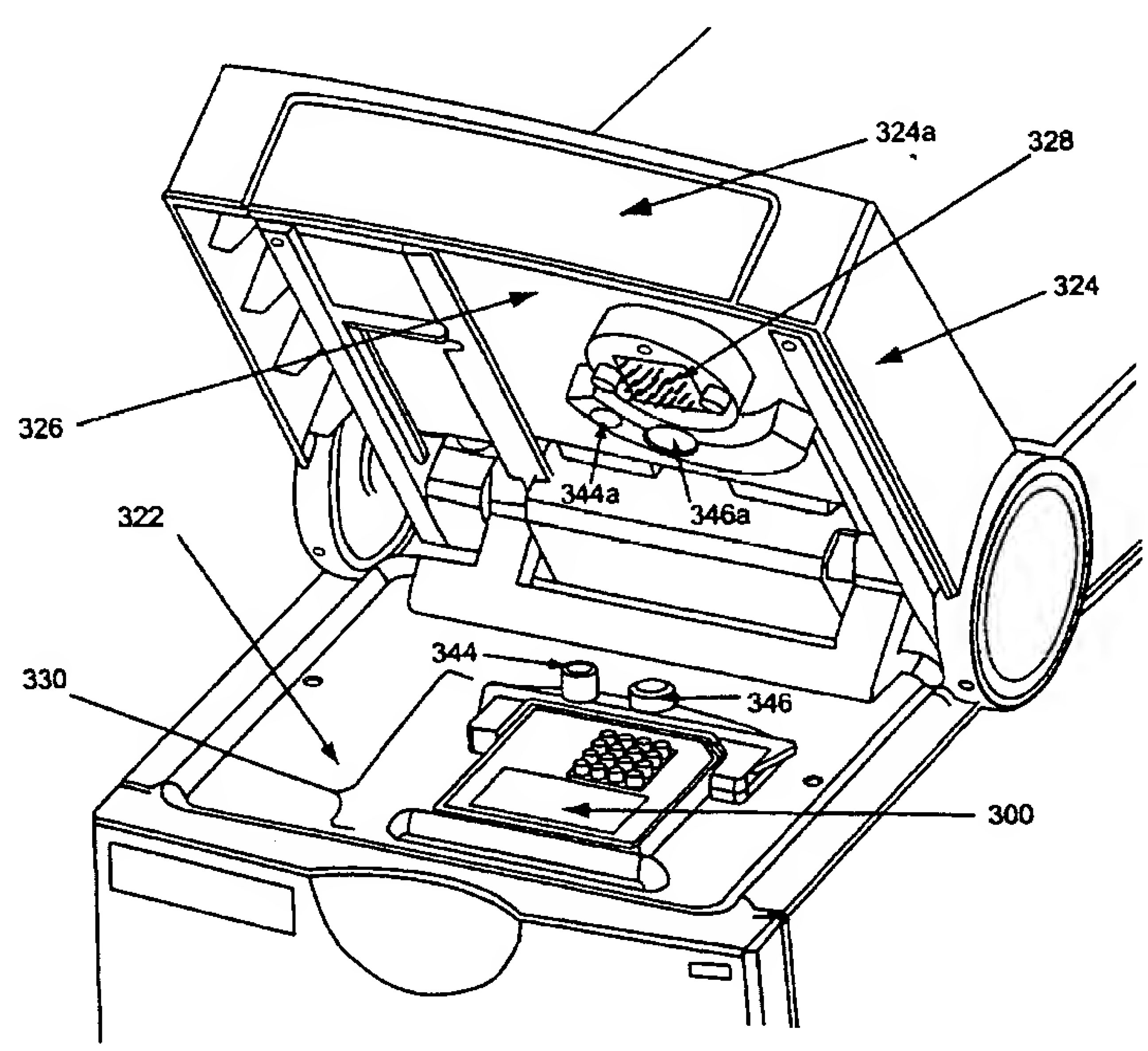
(54) Title: INDICATOR COMPONENTS FOR MICROFLUIDIC SYSTEMS



(57) **Abstract:** Microfluidic devices and systems that include keying, registration or indication elements that communicate a functionality of the microfluidic device to the instrumentation which is used in conjunction with these devices. Indicator elements include structural indicators, electrical indicators, optical indicators and chemical indicators. Different indicator elements are indicative of different functionalities, e.g., applications, new vs. used, and the like.

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INDICATOR COMPONENTS FOR MICROFLUIDIC SYSTEMS

BACKGROUND OF THE INVENTION

Microfluidic devices and systems have advanced rapidly from academic postulations to functioning commercial research products that are actively contributing to the research and development of pharmaceutical and other biotechnological and chemical products.

Examples of microfluidic devices and systems for performing a variety of different operations are described in, e.g., WO 98/00231, WO 98/05424, WO 98/22811, WO 98/46438 and WO 98/49548, all of which are incorporated herein by reference in their entirety for all purposes. Such microfluidic systems are generally configurable to perform virtually any operation, assay or experiment previously performed at the laboratory bench, but with a greater degree of accuracy, speed and automatability. Specifically, because microfluidic systems are performed in such small spaces, reagent quantities, an mixing times are substantially reduced. Further, because of the integrated nature of microfluidic systems, e.g., channel networks fabricated in a single chip, multiple different operations can be incorporated into a single device and controlled by an automated control and detection system. The availability of automated instrumentation, in turn, provides for unparalleled reproducibility as compared to bench scale operations, which rely upon measurements and judgements of human operators.

It is generally desirable to be able to automate more and more operations that are to be performed within a laboratory. While microfluidic systems, in general, contribute substantially to this automation desire, there exits a number of other operations that can be automated in conjunction with the use of these devices. The present invention provides apparatuses systems and methods that further contribute to this automation trend.

SUMMARY OF THE INVENTION

In a first aspect, the present invention provides a microfluidic device comprising a body structure configured to interface with a base instrument. The body structure includes microfluidic elements and an indicator element fabricated into the body

As used herein, a "functionality" of a microfluidic device refers to the use to which the device will be or has been put. The indicated functionality of a device may range from the relatively general, e.g., for performing multi-sample separations, to more specific, e.g., performing kinetic assay on a protein kinase sample. Thus, as typically used, the functionality refers to the application for the device. However, the term "functionality" as used herein, also includes whether a device is functional for any application in the first instance, e.g., whether the device is nonfunctional as a previously used device.

Typically, from application to application, microfluidic devices and systems rely upon many of the same means to carry out the desired operation, e.g., in fluid or material movement, mixing etc., as well as detection of operation results. As such, instrumentation for operating these systems is generally standardizable, with the devices themselves, the chemistries placed in those devices, and the timing of reagent mixtures yielding distinctions between different operations.

For these standard instruments, different operating parameters, e.g., for performing different operations must generally be preprogrammed into the instrument or computers that control operation of the instruments. Of course it is still incumbent upon the user to identify for the instrument when a different application is to be performed. In accordance with the present invention, however, a microfluidic device is configured with an indicator element which indicates to the instrument the functionality of the device that is interfaced with the instrument, e.g., the specific type of assay or other application that is to be performed, or whether the device has been previously used. The instrument then typically adjusts for carrying out the operation of the device interfaced with it. For example, the instrument may select from different available detection modes, e.g., fluorescence wavelengths, UV transmittance, etc., as well as different available material transport means, e.g., pressure based fluid transport, electrokinetic transport or hybrid pressure/electrokinetic systems. For specifically identified functionalities, e.g., specific separations, enzyme assay or the like, the instrument also optionally implements control profiles, e.g., a script for directing fluids or other materials through specific channels at specific times and/or in specific ratios, volumes and/or flow rates.

An overall system including a microfluidic device and its associated instrumentation is illustrated in Figure 1. As shown, the system includes a microfluidic device 100, which is selected from a menu of devices having different functionalities, e.g., devices 100-106. As described in greater detail below, the microfluidic device typically

assembled from an aggregation of planar layers to form a single integrated microfluidic device that includes the channels and chambers within its interior portion.

One example of a microfluidic device is illustrated in Figure 2. Specifically, Figure 2 illustrates the layered construction of preferred microfluidic devices. As shown, the device body structure 200 is fabricated from two or more layers 202 and 208. In particular, the bottom portion of the device 202 comprises a solid substrate that is substantially planar in structure, and which has at least one substantially flat upper surface 204. The channels and/or chambers of the microfluidic devices are typically fabricated into the upper surface of the bottom substrate or portion 202, as microscale grooves or indentations 206, using the above described microfabrication techniques. The top portion or substrate 208 also comprises a first planar surface 210, and a second surface 212 opposite the first planar surface 210. In the microfluidic devices prepared in accordance with the methods described herein, the top portion also includes a plurality of apertures, holes or ports 214 disposed therethrough, e.g., from the first planar surface 210 to the second surface 212 opposite the first planar surface.

The first planar surface 210 of the top substrate 208 is then mated, e.g., placed into contact with, and bonded to the planar surface 204 of the bottom substrate 202, covering and sealing the grooves and/or indentations 206 in the surface of the bottom substrate, to form the channels and/or chambers (i.e., the interior portion) of the device at the interface of these two components. The holes 204 in the top portion of the device are oriented such that they are in communication with at least one of the channels and/or chambers formed in the interior portion of the device from the grooves or indentations in the bottom substrate. In the completed device, these holes function as reservoirs for facilitating fluid or material introduction into the channels or chambers of the interior portion of the device, as well as providing ports at which electrodes may be placed into contact with fluids within the device, allowing application of electric fields along the channels of the device to control and direct fluid transport within the device.

These devices may be used in a variety of applications, including, e.g., the performance of high throughput screening assays in drug discovery, immunoassays, diagnostics, genetic analysis, and the like, e.g., as described in Published International Patent Application No. 98/00231 and U.S. Patent No. 5,779,868 each of which is hereby incorporated by reference in its entirety for all purposes.

Figure 3 schematically illustrates an example of a registration/indicator structure on a microfluidic device and its controller/detector instrument. Figure 3A illustrates the microfluidic device 300 that includes a number of exemplary registration structures, from a number of views (top, side, end and perspective). As shown, the device 300 includes a body structure 302 which includes a microfluidic substrate attached or integral thereto (not shown). The body structure includes ports or reservoirs 304 disposed thereon which are in fluid communication with the channel elements of the microfluidic device. The body structure of the device also includes a number of registration structures, e.g., notch 306 and truncated corner 308, which provide an indication of the functionality of the microfluidic device, e.g., the particular application for which the device is used, i.e., nucleic acid separations, protein separations, enzyme assays, cellular function assays and the like. Specifically, the position, number and or size of the registration structures is typically varied from a device of one functionality to a device of another functionality. For example, although illustrated with a single notch 306 along one edge of the body structure 302, multiple notches, or different size notches are optionally used along the same edge or different edges of the body structure to identify the functionality of the overall device.

A complementary structure or set of structures on the instrument is used to ensure that the instrument is appropriately configured to interface, control and monitor the functionality, e.g., the application, of the microfluidic device inserted therein. Figure 3B illustrates a portion of an example of a controller detector instrument 320 that includes a nesting region 322 onto which the device 300 is mounted.

A lid 324 is rotatably attached to the instrument 320. The underside of the lid 326 typically includes a number of interface elements for controlling the functioning of the device. For example, as shown, a plurality of electrodes 328 are provided attached to the underside 326 of the lid 324. These electrodes 328 rotate into communication with fluids in the reservoirs 304 in the body structure of device 300. These electrodes 328 that are operably coupled to power sources (not shown) within the instrument 320, provide actuation of material movement within the channels of the device 300 via electrokinetic forces. Although shown as electrodes 328, other interfaces are optionally or additionally provided in the lid. For example, in certain preferred aspects, one or more vacuum or pressure ports are provided in the lid with appropriate connectors for interfacing with one or more reservoirs 304 of the device 300, in order to provide material movement by pressure induced flow. These vacuum or pressure ports are operably coupled to vacuum or pressure

taller than post 346. With reference to Figure 3B, these posts 344 and 346 are positioned to mate with corresponding apertures or cavities 344a and 346a, respectively, in interface cassette 324a or optionally lid 324. The complementary nature of posts 344, 346 and cavities 344a and 346a, ensures that the interface cassette 324a inserted into lid 324 is appropriate for the particular device 300, as indicated by the registration structures on barrier 336, e.g., notch 306, and posts 344 and 346. In preferred aspects, a portion or all of barrier 336 is removable (e.g., barrier portion 336a), allowing for substitution with a barrier that includes different registration elements, e.g., numbers and sizes of notches, posts and the like. In operation, microfluidic devices having different functionalities include different registration structures on their body structure, which registration structures are indicative of the functionality of the device. When a device having a different functionality is to be run on an instrument, one replaces the barrier 336 with a new barrier having registration structures complementary to the functionally desired device, and also substitutes the interface cassette with an appropriate interface for the new device, e.g., electrode configuration, vacuum or pressure ports, etc. Certain of the registration structures on the cassette 324a and barrier 336 cooperate to ensure that both the cassette and the barrier are appropriate for the device to be run. Improper cooperation of these elements can lead to damaging of elements of the device and/or the interface cassette, e.g., bending electrodes, damaging optics, etc. Proper alignment of the microfluidic device in the nesting region is shown in Figure 3D.

Thus, in accordance with the above-described aspect of the present invention, “indication of a device’s functionality to the instrument” is provided by an ability to close lid 324 over the device 300, e.g., improper interfacing of a device and an instrument is prevented by structural interference of one or more of the registration elements, e.g., as between device 300 and barrier 336 and/or between barrier 336 and interface cassette 324a. Thus, this “indication” encompasses both more active communication between the device and the instrument, as described in greater detail herein, as well as passive communication, e.g., as described with reference to Figure 3.

Figure 4 schematically illustrates alternate examples of a microfluidic device having mechanical indicator or registration elements, as described herein. As shown, a microfluidic device body structure 400 (shown from a side view), is provided having a series of notches 404-412 disposed in its lower surface 402. The arrangement, size and shape of these notches 404-412 is selected depending upon the particular application or

the body 400, e.g., notches 404-412 deflect the posts in a pattern reflective of those indicator structures, e.g., only posts 466, 470-476, 482-486 and 490-492 are deflected. The deflection or lack of deflection of each post is detected by the instrument. As a result, the functionality of the device, as indicated by the arrangement, size and position of notches (or other indicator structures), is communicated to the instrument by virtue of the number and identity of the posts that are deflected by the body of the device. In this latter aspect, the "indication" of a device's functionality is more of an active communication between the device and the instrument, e.g., by virtue of the device's active deflection of certain structures ("switches") on the instrument. The instrument then configures itself, e.g., via software or firmware programming, to run the device mounted thereon.

In alternate aspects, the indicator elements fabricated into or otherwise disposed on or within the microfluidic devices, comprise electrical indicator elements. The electrical indicator elements described herein may be passive or active electrical elements. In preferred aspects, the electrical indicators are passive, e.g., having no internal power supply such as a battery, due to the costs associated with such systems. While not preferred, it will be appreciated that active electrical indicator elements are also envisioned within the scope of the present invention.

Typically, electrical indicator elements comprise one or more electrical circuits disposed on or within the body of the microfluidic device. The electrical circuits are typically oriented to contact two or more electrical contacts disposed upon the nesting region of the controller instrument, so as to complete an electrical circuit between the two or more contacts. The indicator function of the electrical indicator elements is optionally provided by the number and identity of different circuits that are completed when the device is inserted into the nesting region. Specifically, the pattern of electrical circuits connects a distinct set or subset of electrical contacts in the nesting region to yield an electrical signature that is indicative of the functionality of the device used. Alternatively, the specific resistance or conductivity of the electrical circuits on the device is varied among different devices, such that this resistance level comprises the electrical signature that is indicative of the functionality of the device.

Fabrication of electrical circuits into or on a device's body may be accomplished by a number of means. For example, in some aspects, simple patterned metal layers are disposed upon an outer surface of the body so as to contact a preselected subset of electrical contacts disposed upon the nesting region, thereby yielding a preselected electrical

current between two separate contact pads, the level of resistance of those circuits, or both. By way of example, in the device shown in Figure 5, an electric current could be applied between contact pads 554 and 558, e.g., via circuit/wire 566, and between pads 562 and 564, via circuit/wire 568. However no other currents could be applied or detected due to the lack of an existing circuit. Additionally or alternatively, the electrical resistance in the existing circuits is optionally varied as an indicator function. This increases the variability of the signaling function.

As noted above, one or more of the electrical circuits, e.g., wires 566 and 568 comprises a fused link. Such fused links are generally provided such that a known level of electrical current will excessively heat the wire, resulting in its melting and severing. These circuit compositions are well known to those of skill in the electronics arts.

Although illustrated as an array of contact pads connected by wires or metal traces, it will be appreciated that in preferred aspects, an integrated circuit is used to provide the electrical circuits on the body of the device. Specifically, the complexity of circuits available through IC technology allows substantially greater variability in an electrical indicator element. Further, such ICs are readily incorporated into the body of the devices of the invention, e.g., in the same fashion the microfluidic device substrate is attached to the holder assembly 502 in Figure 5. Electrical interaction with the nesting region is then accomplished in the same fashion as shown in Figure 5, or alternatively, through the inclusion of electrical connector pins, i.e., as typically used in the electronics industry for connecting ICs to circuit boards.

In a further aspect, the indicator element fabricated into or otherwise disposed on the body of the microfluidic device comprises an optical indicator element. As used herein, an optical indicator element is an element that is optically detected by the instrument. Again, as with the electrical indicator elements described above, optical elements may be passive or active, e.g., emitting detectable light levels. Typically, however, passive optical indicators are preferred. One example of a particularly preferred type of optical indicator element is a bar code that is affixed to or otherwise attached or fabricated onto the microfluidic device's body structure. Specifically, bar codes may be readily employed as indicators of the particular assay or other functionality of the microfluidic device being used. Instruments used in conjunction with those devices that incorporate include detection systems for detecting the optical indicator elements. In the case of bar codes, suitable and well known bar code readers are incorporated into the

What is claimed is:

1. A microfluidic device, comprising:

a body structure configured to interface with a base instrument, the body structure having microfluidic elements disposed therein; and

an indicator element fabricated into the body structure, the indicator element providing an indication to an instrument of a functionality of the microfluidic device.

2. The microfluidic device of claim 1, wherein the indicator element provides an indication as to whether the device has been previously used.

3. The microfluidic device of claim 1, wherein the indicated functionality of the microfluidic device is a specific application of the microfluidic device.

4. The microfluidic device of claim 3, wherein the indicated functionality comprises a specific assay type to be performed within the microfluidic device.

5. The microfluidic device of claim 1, wherein the indicated functionality of the microfluidic device comprises a desired flow control system for use with the microfluidic device.

6. The microfluidic device of claim 1, wherein the indicator element is selected from a mechanical indicator element, an electrical indicator element, an optical indicator element, and a chemical indicator element.

7. The microfluidic device of claim 6, wherein the indicator element comprises a mechanical indicator element, the mechanical indicator element comprises a registration structure, the registration structure having a shape or size indicative of a functionality of the microfluidic device.

and a detector disposed within the controller instrument with a microfluidic device placed in the nesting region; and

a microfluidic device having a body structure, the body structure comprising an indicator element, the indicator element providing an indication to the instrument of a functionality of the microfluidic device.

17. The microfluidic system of claim 16, wherein the indicator element is selected from a mechanical indicator element, an electrical indicator element, an optical indicator element, and a chemical indicator element.

18. The microfluidic system of claim 17, wherein the indicator element comprises a mechanical indicator element.

19. The microfluidic system of claim 18, wherein the indicator element comprises a first registration structure having a first selected size or shape, and wherein the nesting region comprises a second registration structure that is complementary to the first registration structure.

20. The microfluidic system of claim 19, wherein positioning of the microfluidic device on the nesting region such that the registration structure on the microfluidic device and the complementary registration structure are joined, the microfluidic device is oriented to operably interface with the interface array.

21. The microfluidic system of claim 19, wherein the first selected shape is selected based upon an application for which the microfluidic device is intended.

22. The microfluidic system of claim 19, wherein the first registration structure is selected from a tab, a series of tabs, a pin, a series of pins, a hole disposed in the body structure, a series of holes in the body structure, a notch in the body, a series of notches in the body, and a shaped edge of the body.

31. The microfluidic system of claim 17, wherein the indicator element comprises an optical indicator element, the optical indicator element being detectable by the instrument to indicate to the instrument the functionality of the microfluidic device.

32. The microfluidic system of claim 31, wherein the optical indicator element comprises a bar code, and wherein the controller instrument comprises a bar code reader.

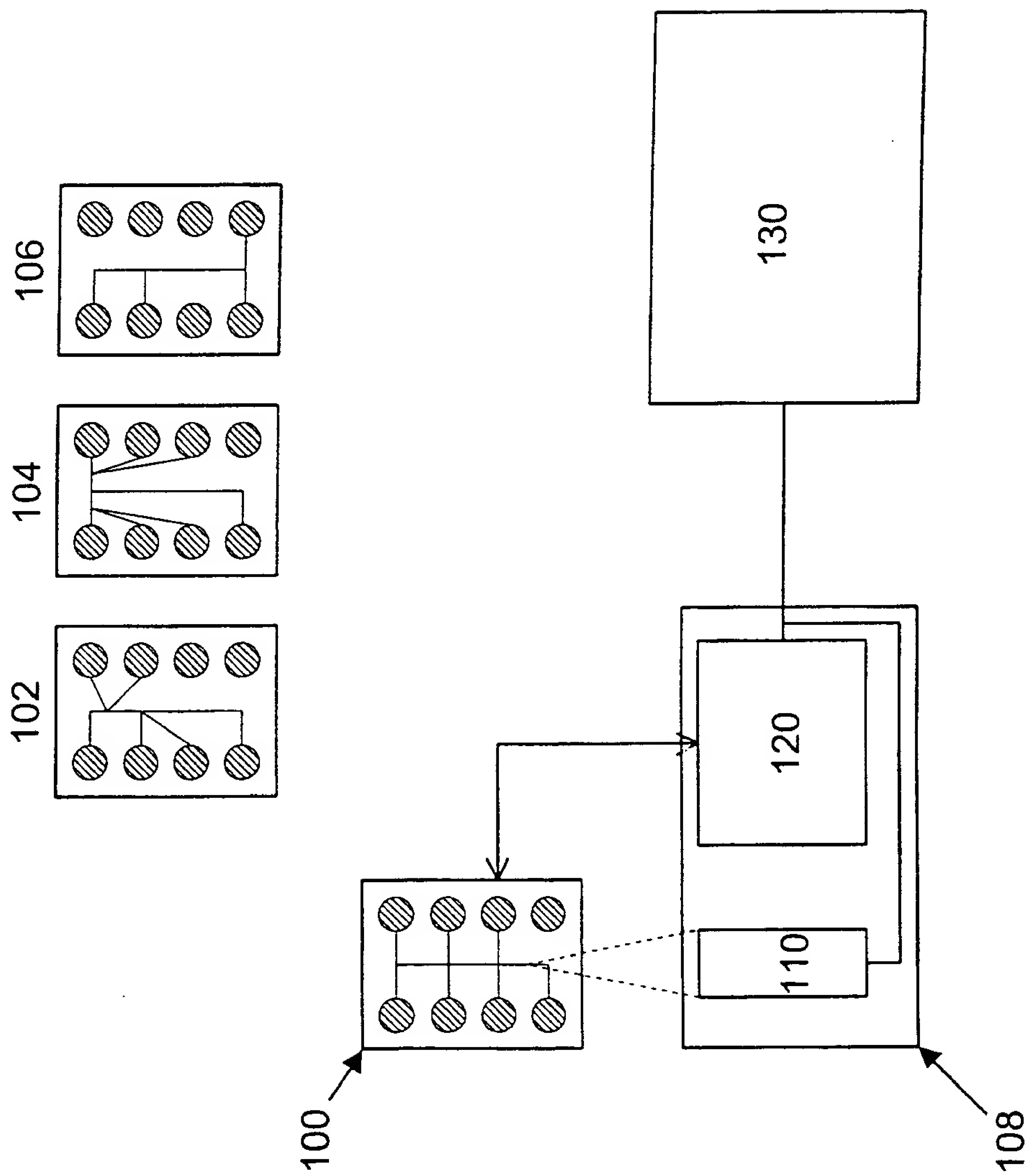

Fig. 1

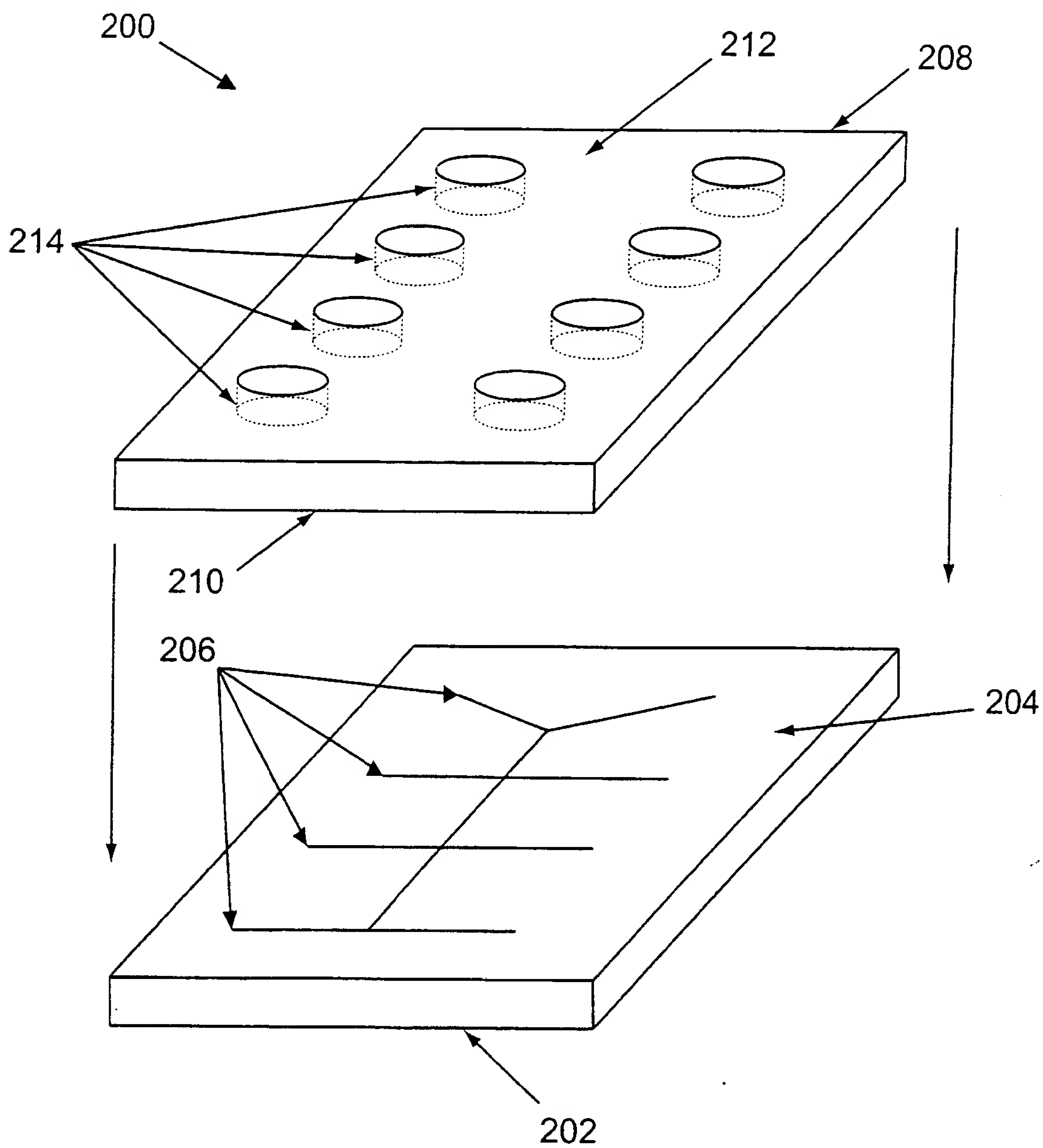

Fig. 2

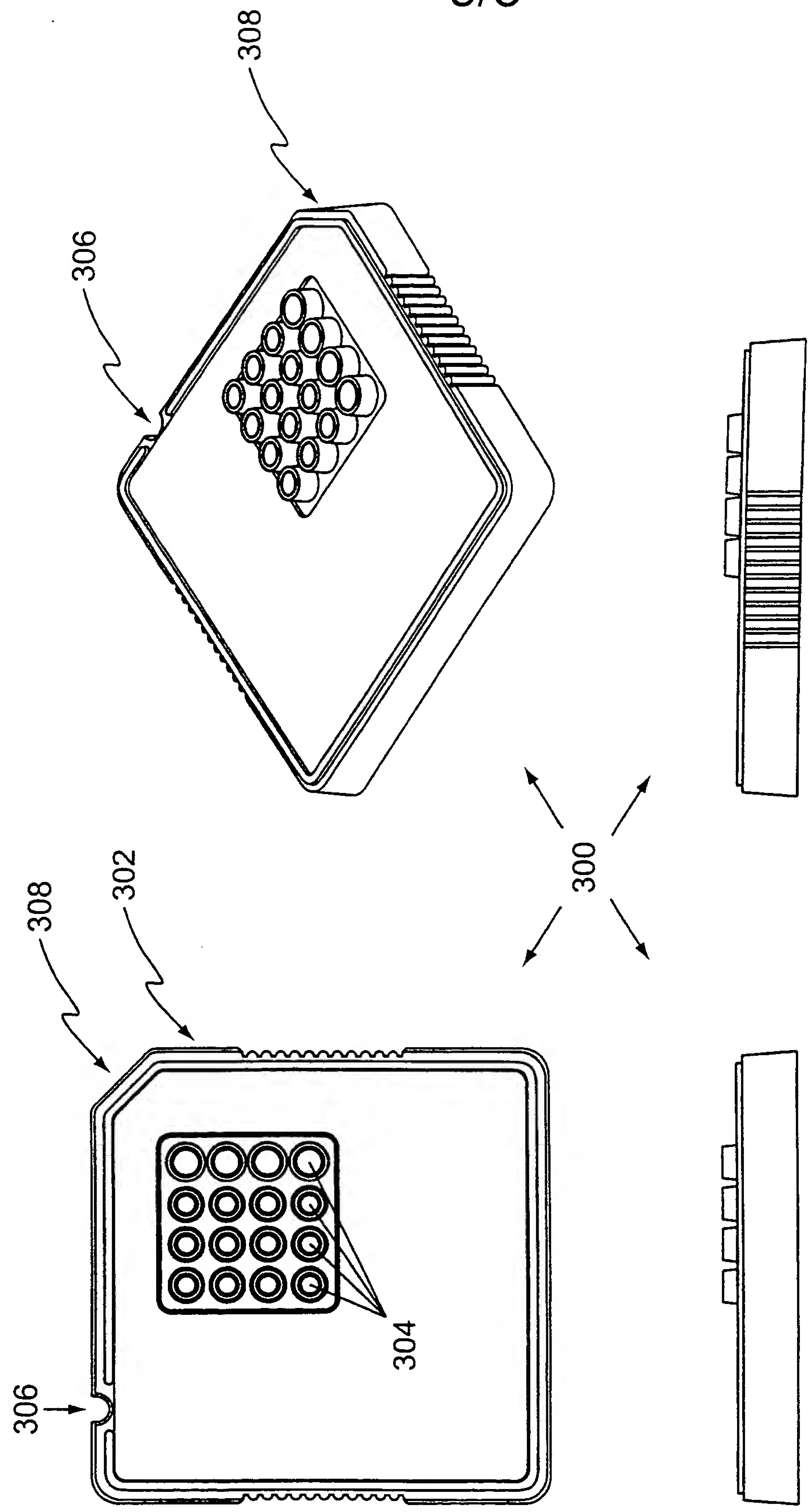

Fig. 3A

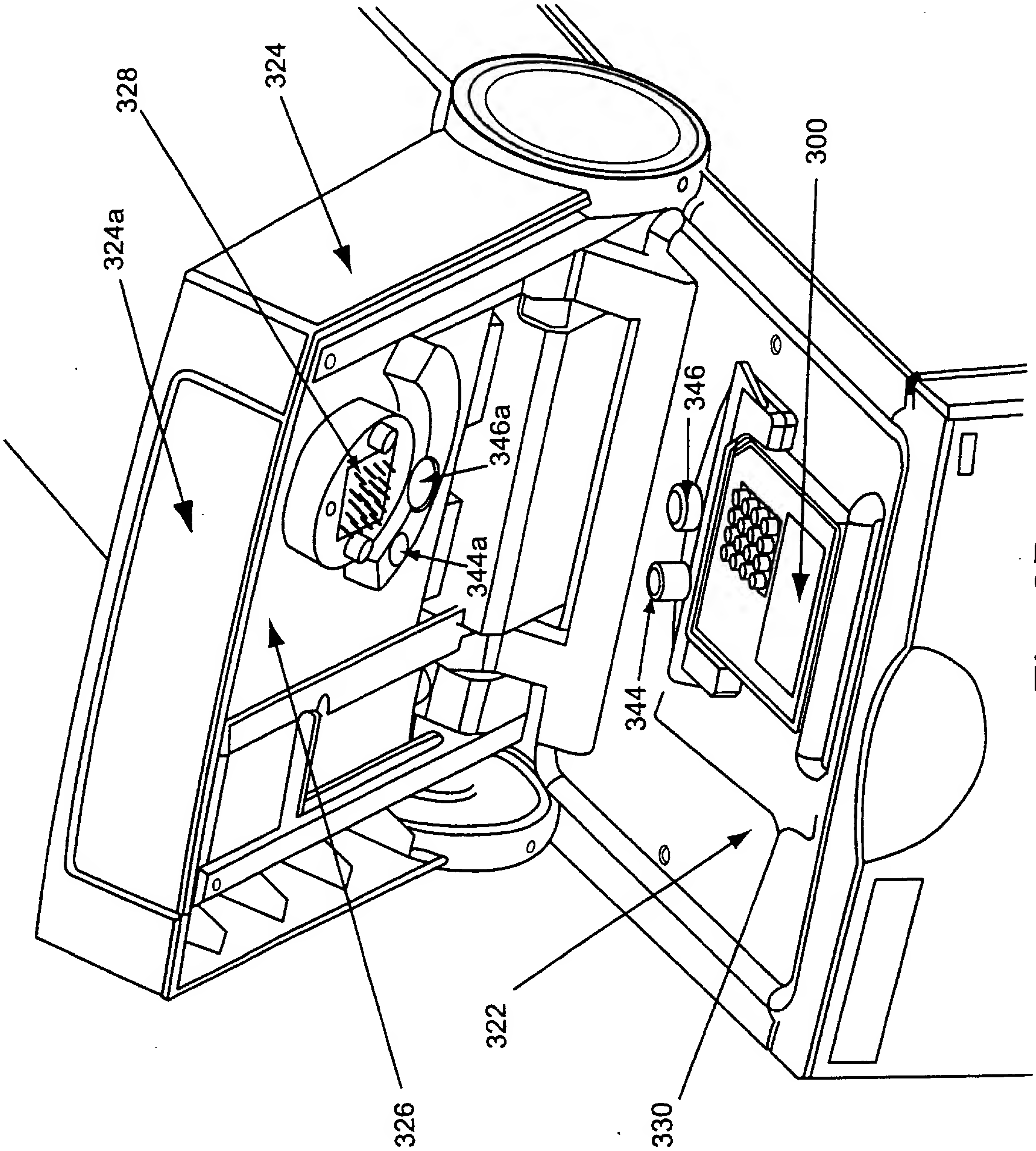

Fig. 3B

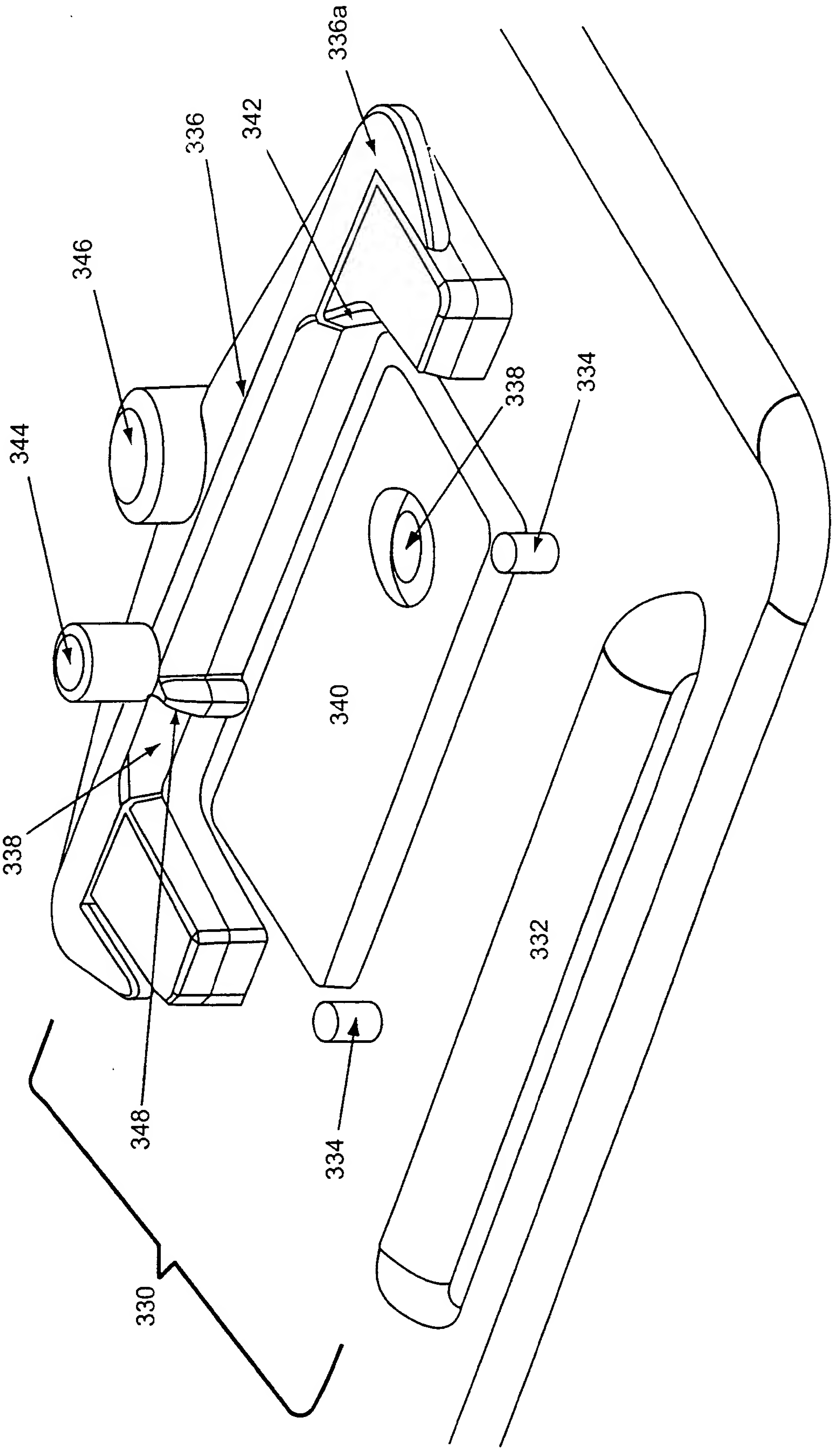

Fig. 3C

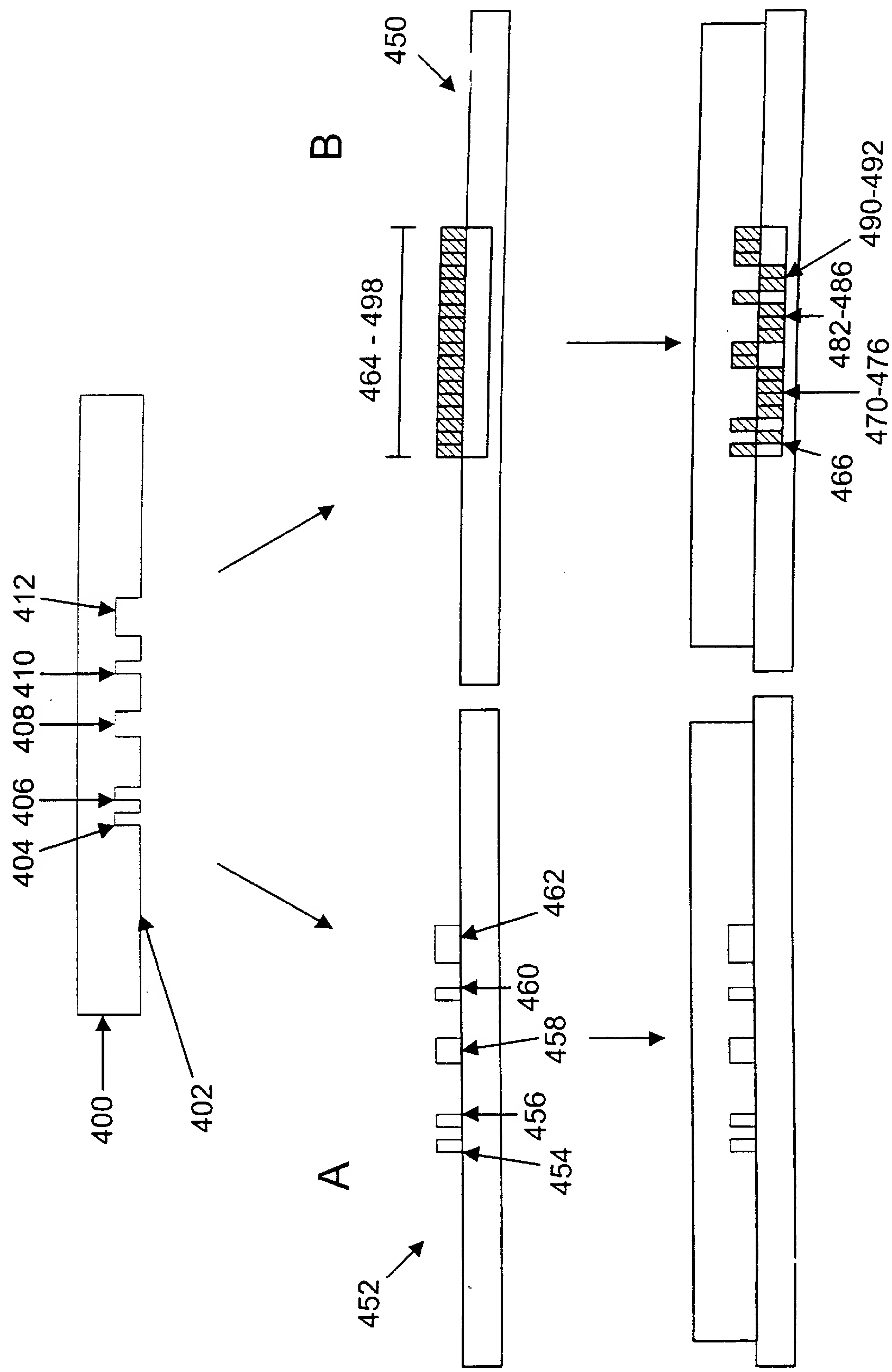
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Fig. 4

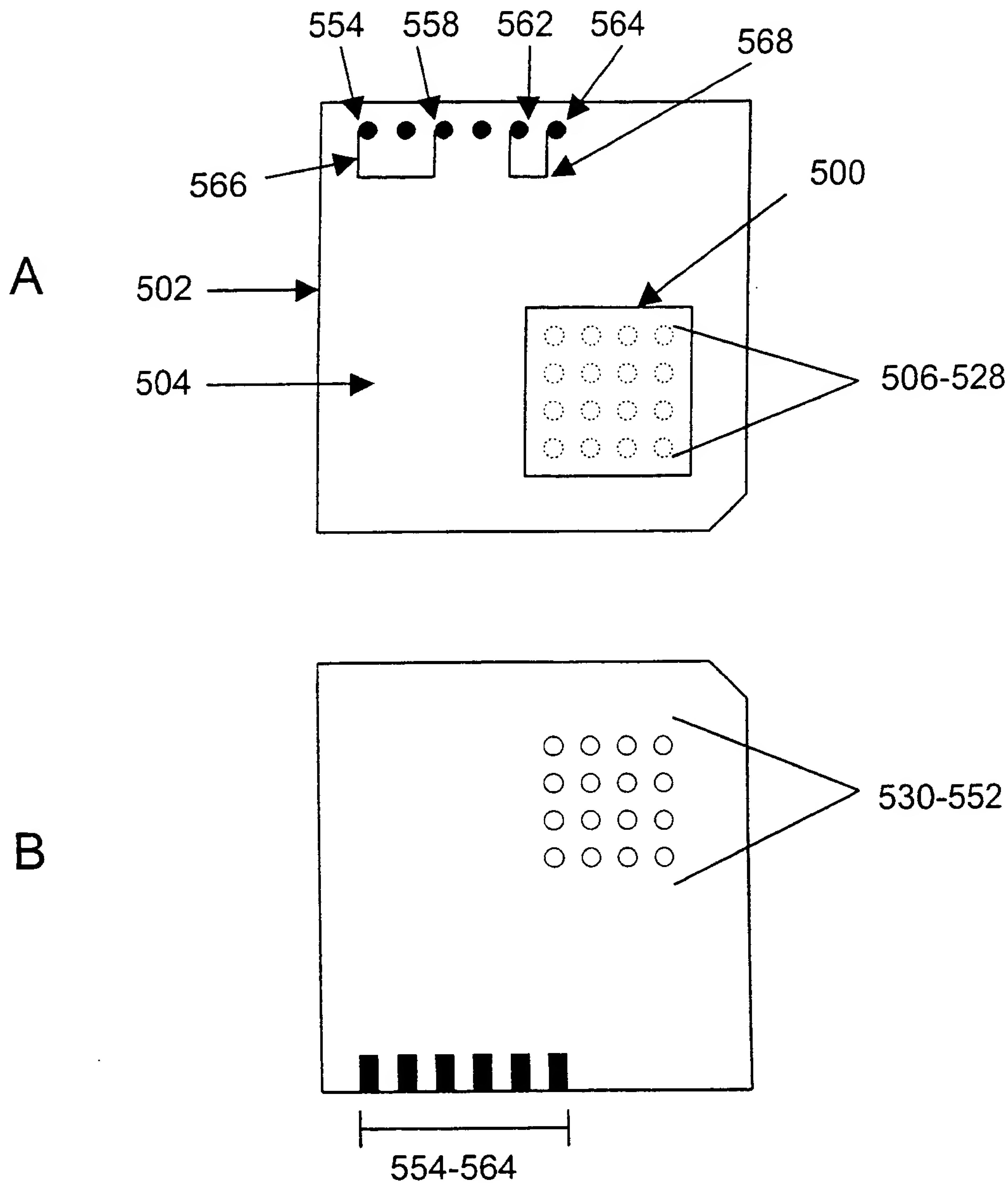

Fig. 5

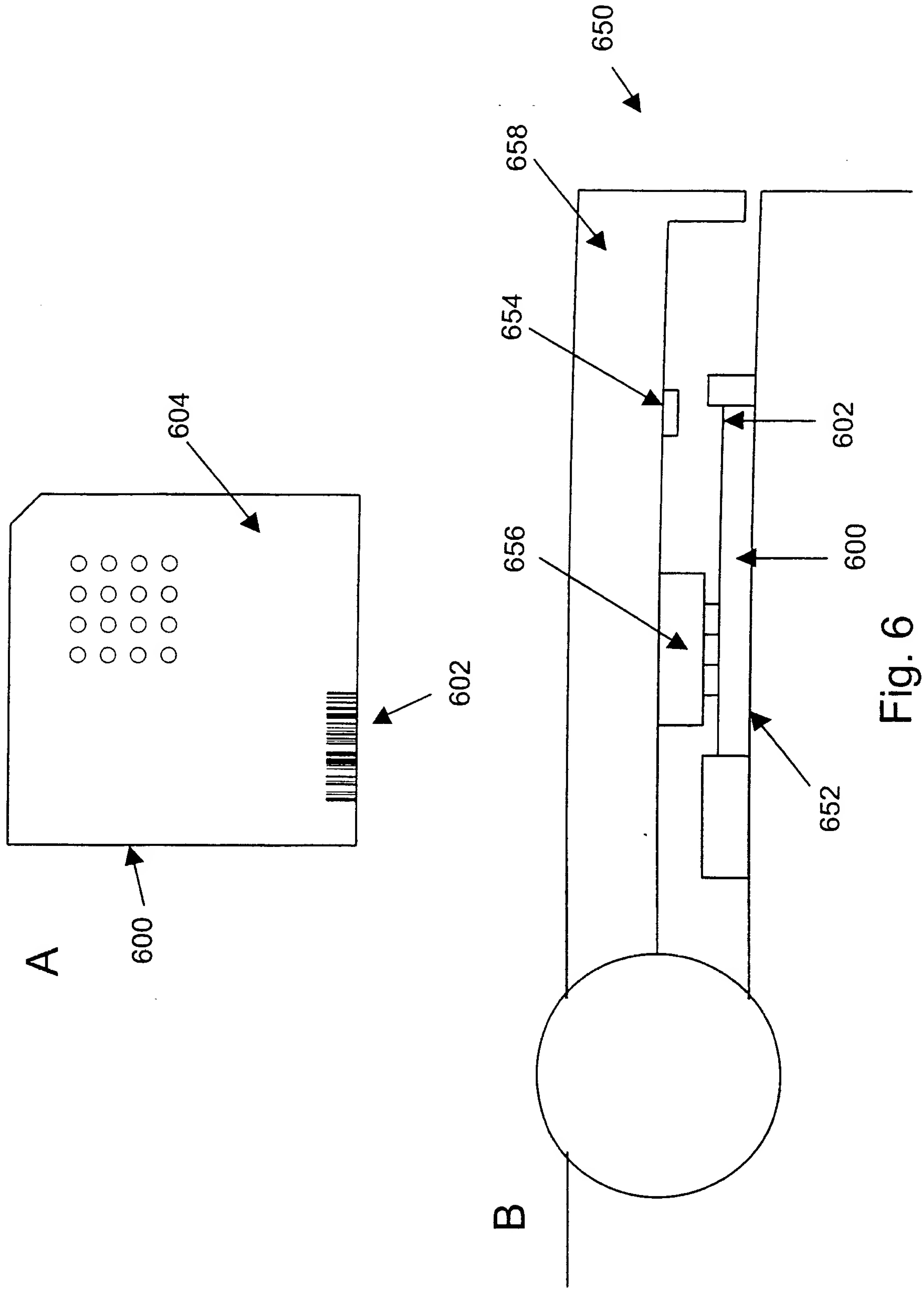

Fig. 6

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/22147

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L B01J C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	page 17, line 36 -page 21, line 28 figures 1,2 ---	10,12, 24,26, 29,30

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
7 November 2000	14/11/2000

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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